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EXAMINER	
TON, THAIAN N	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/821,200	Applicant(s) SCHATTEN ET AL.	
	Examiner Thaian N. Ton	Art Unit 1632	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-84* is/are pending in the application.

4a) Of the above claim(s) *22,23,28-49 and 67-84* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21,24-27 and 50-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *4/9/04; 9/2/04* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/2/04;1/19;1/27*.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

Claims 1-84 are pending; claims 22, 23, 28-49, 67-84 are withdrawn; claims 1-21, 24-27, 50-66 are under current examination.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-21, 24-27, 50-66) in the reply filed on 6/1/06 is acknowledged. The traversal is on the ground(s) that it is not an unreasonable burden on the Patent Office to formulate a search drawn to methods of nuclear transfer wherein the blastomeres are cultured to produce stem cells. Applicants argue that these claims are interrelated and thus, request reconsideration of the Restriction requirement. This is not found persuasive because the methods of producing stem cells require a separate and materially different protocol, which require different technical considerations, reagents, and result in a materially different product. Furthermore, of the two inventions are classified separately, and has acquired a separate status in the art due to their divergent subject matter. Thus, it is maintained that it would be undue to search both Inventions I and II together.

The requirement is still deemed proper and is therefore made FINAL.

Claims 22, 23, 28-49, 67-84 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 6/1/06.

Information Disclosure Statement

Applicants' IDS, filed 9/2/04, 1/19/05, and 1/27/06, have been considered.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-21, 24-27, 50-66 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim1, 10, 34-53 of copending Application No. 11/003,006 in view of Campbell [**Cloning & Stem Cells**, 3(4):201-208 (2001)].

The instant claims are directed to introducing nuclei with one or more molecular components into an egg, culturing the egg to produce a viable embryo and transferring the embryo to the oviducts of a female and producing a cloned animal. The instant claims differ from the '006 claims with regard to the type of egg used. The instant claims recite the term "egg" and the '006 claims recite the term "extrusion enucleated egg". However, Campbell provide teachings to show that "Successful development [of the NT unit] is dependent upon numerous factors, including type of recipient cell, source of recipient cell, method of reconstruction, activation, embryo culture, donor cell type, and donor and recipient cell cycle

stages." See *Abstract*. Campbell teaches that metaphase II [MII] oocytes are considered the cytoplast of choice because the genetic material is arranged upon the meiotic spindle and easily removed [see p. 202, 2nd column, 1st ¶], further, following introduction of the donor somatic cell into an enucleated oocyte, activation must occur to induce further development and the timing of this activation in relation to NT has been implicated in the ability of the NT unit to develop further [see p. 203, 2nd col.].

Thus, given the instant claims in view of Campbell, it would have been obvious for one of skill in the art to use an extrusion-enucleated oocyte in the methods of the '006 claims.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 24-27 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are directed to animals produced by methods of nuclear transfer. Specific embodiments limit the animal to primate (claim 25), non-human primate (claim 26) and human (claim 27). Animals that are produced by nuclear transfer would not be distinguished from naturally occurring animals, and thus, are non-statutory subject matter. Furthermore, the claims encompass human beings, which is also non-statutory subject matter. See 1077 O.G. 24, April 21, 1987. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206, USPQ 193 (1980). See also, MPEP § 2105.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-21, 24-27, 50-66 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention. The claims are directed to methods of introducing nuclei along with one or more molecular components into an egg; culturing the egg to produce a viable embryo; transferring the embryo to the oviducts of a female; and producing a cloned animal. Specific embodiments teach that the nuclei have desired characteristics, such as one that is linked to a specific disease or disorder. Further embodiments are directed to performing this method using somatic cell nuclear transfer (SCNT). Other claimed embodiments are directed to animals produced by this method.

Breadth of the claims. The claims broadly read on methods of introducing donor nuclei into recipient eggs by methods other than SCNT, using a donor nuclei

and recipient egg of the same or different species of animal, using any type of donor nuclei and any type of recipient egg, to produce any cloned animal.

Guidance of the Specification/The Existence of Working Examples. The specification teaches that the limitations associated with performing SCNT in primates is that removal of the donor egg DNA, along with the spindle and spindle proteins, cause the SCNT reconstituted oocyte to no longer form a functional bipolar mitotic spindle at first mitosis (see p. 3, paragraph 0008). The working examples are directed to nuclear transfer methodology, using enucleated rhesus monkey oocytes as recipient cells, and various donor sources, including granulosa, endothelial cells from rhesus umbilical cord, isolated, cultured ICM cells derived from rhesus blastocysts, and primary rhesus fibroblast cell lines. The NT constructs were activated and cultured, the resultant embryos were transferred in surrogate rhesus females, NT units were also analyzed by immunocytochemistry (see Example 1). The specification provides no guidance with regard to any implantation or pregnancies that resulted from NT constructs transferred to surrogate mothers. The specification teaches the observation that the primate embryos had faulty mitotic spindles, particularly, with regard to a defective NT mitotic spindle with misaligned chromosomes centrosomal NuMA (nuclear mitotic apparatus protein) at meiosis and mitosis. See Figure 2. The specification teaches that previously there has been no evaluation of the centrosomes or structural/molecular motor proteins role in bipolar spindle assembly after NT, and that the dysfunctional centrosomes, as well as missing NuMA and HSET kinesin result in mitotic multipolar spindles with misaligned chromosomes and aneuploid embryos after NT. See page 11, paragraph 43 of the specification. Thus, the invention relates to correcting these spindle defects, for example, by the evaluation of mechanisms for potential NT failures due to mitotic error, providing key components needed for the correction of mitotic spindle defects, including NuMA and HSET kinesin. See page 12, paragraph 47.

State of the Art/Predictability of the Art. The claims are broadly drawn to cloning of any animal. However, the state of the art for production of any non-human mammal is not found to be predictable, utilizing any somatic cell donor, as instantly claimed. For example, Oback (**Cloning & Stem Cells**, 4(2):147-168 (2002)) who review the state of the art for donor cells used in cloning and state, "Currently, we do not know what makes a good donor cell. In mammals, more than 200 distinct cell types are plainly distinguishable by morphology and more will probably be discovered when better molecular markers become available. Less than 5% of these have been tested as nuclear donors, and they all support development to blastocysts; however, many repeatedly failed to generate viable offspring." See p. 147, 2nd column, 1st ¶. Oback further supports the lack of teachings provided in the art with regard to donor cells that predictably result in live offspring by showing that in different animal species, different somatic donor cells have been tested with varying results. For example, Wakayama and Yanagimachi tested eight cell types in NT methodology in mice, and found that live offspring were obtained from fibroblast, undefined fetal gonadal and cumulus cells. Further, Kato tested somatic donor cells in cattle and found that all supported development to blastocysts but live offspring were only obtained from cumulus, oviduct, skin and liver cells. See pp. 155-156 of Oback. Further, Oback teaches that deciding which cell to use as a donor cell in NT methods is not clear because the cells that have worked in certain species are not the same cells that work in other species, and that they are often dissimilar in their cell cycle stage and their cloning competence. Oback provide a summary of cloning efficiencies from various somatic donor cells (see Table 1). It is noted that different cell types provide different cloning efficiencies with regard to different animal species. Thus, when taken with the specification's lack of teachings or guidance to enable the full breadth of the claimed invention (of any cell donor) and the state of the art's clear teaching of the unpredictability of using any

somatic cell as a donor in NT methodology, and the unpredictability amongst species of animals in using different somatic cells, the claims are not enabled.

The unpredictability in the NT art is further supported by the post-filing art of Campbell *et al.* (Reprod. Dom. Anim., 40: 256-268 (2005)) who review the state of the art of NT, and particularly, with regard to the choice of a particular, suitable donor cell, they teach that although different cultured cells, as well as some somatic cells can be used in NT, there are varying results using these cell types, and they state that, "Unfortunately no conclusion can be made on what is the most appropriate cell type for SCNT." See p. 261, Selection & culture of a suitable donor cell. Tian et al. (Reprod. Bio. & Endocrin., I(98): 1-7 (2003)) also support the unpredictability in selection of an appropriate donor cell, they teach that somatic cells have varying cloning competence and that although specific cell types have found to be successful in producing cloned animals, "A clear consensus, however, has not been reached as to the superior somatic cell type for nuclear transfer." They compared various donor cell types from the same donor animal and conclude that the donor cell type can significantly affect embryo development, both *in vitro* and *in vivo*. See pp. 3-4, Cloning competence of various somatic cell types. Thus, specific guidance must be provided to enable the claimed invention in view of the unpredictable state of the art with regard to NT in general, and specifically, for the specific donor cell used.

Li *et al.* (Reprod. Bio. & Endocrin., I(84):1-6 (2003)) state that, "[O]verall efficiency of nuclear transfer is still very low and several hurdles remain before the power of this technique is harnessed. Among these hurdles include an incomplete understanding of biologic processes that control epigenetic reprogramming of the donor genome following nuclear transfer. Incomplete epigenetic reprogramming is considered the major cause of the developmental failure of cloned embryos and is frequently associated with the disregulation of specific genes. At present, little is known about the developmental mechanism of reconstructed embryos. Therefore,

screening strategies to design nuclear transfer protocols that will mimic the epigenetic remodeling occurring in normal embryos and identifying molecular parameters that can assess the developmental potential of pre-implantation embryos are becoming increasing important." See Abstract. Li further state that, "The factors involved in the success of NT are very complex. Although many protocols have been modified and utilized in the NT processes, some events continue to remain ill-defined." See p. 1, last paragraph. This further supports the unpredictability in the art - if it would be routine experimentation to produce cloned animals, then one could expect that any donor cell could be successfully used to produce any species of animal. Such has not been found to be the case. Li *et al.* teach, "The low efficiency and abnormal development of cloned animals are mainly due to incomplete reprogramming and abnormal gene expression.". See p. 2, 1st column, 2nd full ¶. They further state, "[M]ost cloned embryos have been observed to fail to develop to term, and some of the surviving cloned animals have shown abnormalities. The major cause may reside in faulty or incomplete epigenetic reprogramming of the donor nucleus, which affects the gene expression needed for every developmental stage of cloned embryos and offspring. Most cloned embryos lose their developmental abilities during pre-implantation and gastrulation. Moreover, the surviving adults often show abnormalities." See p. 2, col. 1-2, bridging ¶. McEvoy *et al.* (Reprod. Supp., 61 :167-182 (2003)) support this unpredictability, citing that the production of NT-derived ruminants is an inefficient process that generally fails to generate viable offspring. They suggest that after NT, fetal losses are due to significant developmental retardation and placental inadequacies, and state the following, "Indeed, the fact that losses can occur at all stages and in various guises, ranging from gross degeneration of preimplantation embryos to sudden post-natal death of apparently normal offspring, confirms that NT procedures are frequently responsible for fundamental and far-reaching disruption of developmental norms. Intuitively, it could hardly be

otherwise, given that the reconstructed egg comprises a severely traumatized host cytoplasm fused to a donor cell (or nucleus) with which, to a greater or lesser extent, depending on its origin, it is virtually incompatible from the outset. Therefore, the more remarkable phenomenon is that, against the odds, NT sometimes results in the generation of viable offspring." (Emphasis added, p. 173, Nuclear Transfer Technology, paragraphs 2-3). Therefore, NT transfer is clearly not a method that only requires routine experimentation in order to practice, but a complex method that is unpredictable at various stages, as evidenced by the cited art.

The claimed invention, in specific embodiments, is directed to providing molecular components, including NuMA and HSET kinesin during SCNT. This is based upon the specification's observation that the absence of these proteins appear to be the cause for the mitotic spindle defects. However, the post filing art of Chen *et al.* ("Early development of Reconstructed embryos after somatic cell nuclear transfer in a non-human primate," **Theriogenology**, 2006, Article In Press, as of August 2, 2006) show that the removal of the spindle does not appear to be the only cause for the developmental arrest of primate NT embryos. They state that

"So far, only NT of embryonic cells in non-human primates has resulted in live-births. That there has been little success with SCNT in primates is not well understood. According to one report, meiotic spindle removal may be the source of the anomalies; however, that view was dispelled when clinical pregnancies were achieved in the cynomolgus monkey after SCNT embryos were replaced into surrogates. A low rate of blastocyst formation by NT constructs in non-human primates and no live-births underscored substantial problems with SCNT, perhaps due to incomplete nuclear reprogramming of the donor cell." See page 1, Introduction, col. 1-2.

Indeed, Ng *et al.* (**Development**, 131:2475-2484 (2004) show successful pregnancy (but no live-birth) of Long-tailed Macaques. Particularly, they studied embryos that were reconstructed by injecting cumulus and fibroblast cells from the Long-tailed Macaque and Lion-Tailed Macaque (respectively) into enucleated Long-tailed Macaque oocytes. They teach that a spindle from the donor somatic cell was formed 2 hours following NT, and that after activation, the chromosomes segregated

and formed two nuclei. They teach that ninety-three reconstructed embryos were transferred into 31 recipients, which results in 7 pregnancies, but no live-births. See Abstract. Ng *et al.* clearly show the unpredictability found in primate NT, stating that its success is dependent upon the ability of the cytoplast to reprogram the nucleus of the donor cell, or to reverse the epigenetic changes that occur during development, as well as the donor cell that is used. They particularly state that

"[I]t was reported that primates were different from other animals, as disarrayed abnormal mitotic spindles with misaligned chromosomes were formed in all SCNT embryos, and no pregnancies resulted from SCNT embryos transferred into surrogates. It was suggested that meiotic spindle removal may be the source of primate SCNT anomalies, and primate NT appears to be challenged by stricter molecular requirements (NuMA) and Kinsein-related protein HSET for mitotic spindle assembly than does NT in other mammals. ... In this study we describe the first cell cycle changes of SCNT embryos in non-human primates for the first time. Our data demonstrate that SCNT embryos of the non-human primate are similar to other animals in that they can form a normal PCC spindle. We also report early pregnancy failures after embryo transfers of such reconstructed embryos." See pages 2475-6, bridging ¶.

Ng *et al.* teach that the NT embryos were capable of spindle formation (see p. 2477, 2nd col., PCC spindle formation in NT Embryos. Specifically they teach that 14.8% of somatic cell chromosomes will condense into normal PCC spindle within 2 hours of injection, and that these embryos can be implanted and result in pregnancy. They state that, "It also confirms that somatic cell DNA in non-human primates can form a normal PCC spindle after the somatic cell is introduced into a enucleated oocyte." See page 2481, Discussion, paragraphs 1-2. They conclude that the lack of success in producing live-born cloned primates was previously though to be due to removal of NuMA and HSET, but that perhaps the lack of NuMA detection in reconstructed SCNT embryos was due, in part, to technical problems,

such as excessive aspiration of the cytoplasm (see pages 2482-3, bridging ¶). They state that, "Species difference may partially explain the difference, and culture environment may also be a contributing factor, as an optimal medium for SNT has not been reported. In fact, our data supports the conventional belief that incomplete nuclear re-programming is likely to be the reason for the lack of live births in primates." See page 2483, 1st paragraph, last sentence.

Accordingly, in view of the post-filing art of both Chen and Ng, who both show that primate NT is unpredictable, with regard to production of viable embryos or cloned primates, and specifically with regard to Ng's evidence that show that NT non-human primate embryos are capable of spindle formation, one of skill in the art would have to practice undue experimentation to determine what molecular component(s) would need to be added with the nuclei in NT methods, in order to produce a viable primate embryo.

The broad claims do not recite an activation step of the NT unit. However, it is well-known in the nuclear transfer art that activation of the resulting nuclear transfer unit must take place in order to effect further development. However, the claims do not provide such steps. Dinnyés *et al.* [**Cloning & Stem Cells**, 4 :81-92 (2002), reference A11 on Applicants' IDS, filed 9/2/04] report on the state of the art of somatic cell nuclear transfer, stating that, "NT is a complex procedure and each step effects the overall efficiency. The unpredictability of the technology due to biological variation of the recipient oocytes and the donor cells is difficult to control. Therefore, standardization of the steps is important in order to obtain consistent results." See p. 83, 1st column, 2nd full ¶. With particular regard to the importance of activation of oocytes, Dinnyés state that, "In NT, the lack of sperm-induced fertilization steps necessitate the application of an artificial activation in order to trigger further development." See p. 83, 2nd column, last ¶.

The claims also encompass the implantation of cultured nuclear transfer units into surrogate mothers of different species. However, such implantation is not

predictable, as Fehilly *et al.* (**Nature**, Vol. 307, 16 February 1984) teach that often two unrelated species cannot carry a live hybrid fetus to term due to factors such as interspecific pregnancies, placental abnormalities and maternal immunological reaction against foreign antigens of the conceptus which would be the cause of immediate abortion (see p. 634, 1st column, 2nd paragraph). Fehilly *et al.* summarize experiments for the production of such animals, and show an extremely low percentage of full term young (see Table 1, p. 635). Although Fehilly *et al.* show that is possible to produce embryos that have been implanted into surrogate mothers of a foreign species, it is clearly an unpredictable process.

The Amount of Experimentation Necessary. Although the art teaches specific SCNT has been successful in specific species, using specific cells (both donor nuclei and recipient oocytes), the genus of cloning animals by SCNT fails to be enabled by these discrete embodiments. The state of the art clearly shows the undue experimentation would be necessary in order to determine what parameters would be required in order to arrive at producing a live-born, cloned animal, as broadly claimed.

Accordingly, in view of the state of the art of NT, particularly with regard to the unpredictability of donor cells and recipient cells to be used, where the state of the art only supports specific cell types with regard to successful NT, the state of the art of primate NT, wherein art at the time of filing shows that improper spindle formation is perhaps not the only cause for developmental arrest of primate NT embryos, the post-filing art that shows that primate NT remains unpredictable, the lack of teachings or guidance provided by the specification, with regard to the one or more molecular components that would be added to the nuclei to produce a viable embryo, and a resultant cloned animal, it would have required undue experimentation, for one of skill in the art, to determine the parameters, cell types, molecular components necessary to achieve successful SCNT, as broadly claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5, 21, 24, 50-54 and 66 are rejected under 35 U.S.C. 102(b as being anticipated by Schnieke *et al.* (**Science**, 278:2130-2133, 19 December 1997).

The claims are directed to methods of nuclear transfer, wherein the nucleic, along with one or more molecular components are introduced into an egg by somatic cell nuclear transfer (SCNT), culturing the egg to produce a viable embryo and transferring the embryo to the oviducts of a female, and producing a clone animal. In further embodiments, the nucleus has desired characteristics, linked to a specific disease or disorder, wherein the viable embryo is transgenic.

<u>Claim Interpretation</u>. The claims are interpreted as follows: the term molecular components broadly encompasses any molecular component that is introduced along with the donor nucleus. The donor nucleus will inherently contain molecular components. Thus, art that teaches introduction of a donor nucleus is introducing molecular components into the egg.

Schnieke *et al.* teach the production the production of sheep embryos by nuclear transfer, wherein the fibroblast donor cells were co-transfected with a

neomycin resistance marker and the human coagulation factor IX genomic construct (see Abstract and p. 2130, 1st column, 1st paragraph). They teach that the embryos were then transferred to surrogate mothers and live lambs were produced (p. 2131, 1st column, 3rd ¶). Thus, Schnieke *et al.* anticipate the claimed invention, because they teach methods of nuclear transfer, as required by the claims (claims 1-5 and claims 50-54), they teach the production of transgenic embryos (claim 21, 66) , they teach an animal produced by the method (claim 24).

Claims 1-5, 7, 21, 24, 50-54, 56, 66 are rejected under 35 U.S.C. 102(b) as being anticipated by Strelchenko *et al.* (**U.S. Pat. No. 6,011,197**, January 4, 2000, Reference A3 on Applicants' IDS, filed 9/2/04).

Strelchenko teach nuclear transfer for the production of cloned animals (col. 37). They teach that the totipotent cells produced by NT can be transgenic, wherein the recombinant product can encode a polypeptide that confers resistance to one or more diseases (col. 12, lines 16-37). They teach the isolation of transgenic cells to be used in NT methods (col. 13). They teach production of NT embryos, which can then be used for a second NT (col. 40, lines 1-13). They teach that the cloned embryos can then be implanted into surrogate mothers (see col. 41-42, bridging ¶). They specifically teach production of bovine NT embryos using totipotent cells as donor cells, and enucleated bovine oocytes as recipient cells (see col. 46, Example 4) and the second NT of the embryos, and the production of liveborn calves from these embryos (col. 47-48, Example 5).

Accordingly, Strelchencko anticipate the claims, because they teach the introduction of nuclei (which would contain molecular components) into an egg, culturing the egg to produce a viable embryo, and then transferring the embryo to the oviducts of a female to produce a cloned animal.

Claims 1-5, 7, 13, 21, 24, 50-54, 62, 66 are rejected under 35 U.S.C. 102(a) or alternatively, under 35 U.S.C. 102(e) as being anticipated by Collas *et al.* (U.S. Pub. Nno. US 2003/0046722 A1, published March 6, 2003, filed December 21, 2001).

Collas *et al.* teach methods of nuclear transfer, specifically they teach that the donor nucleus is contacted with one or more conditions that allow for formation of a chromatin mass (p. 2, ¶ 0008). They teach that subsequent rounds of nuclear transfer of the resultant NT unit. They specifically teach that a permeabilized donor cell is incubated in a reprogramming media that can add a factor to the nucleus, and then insertion of this cell into an enucleated oocyte. They teach that the reprogramming media can contain a mitotic extract that contains nuclear or cytoplasmic components. (p. 2, ¶ 0009). They teach that the donor cells/nuclei can be transgenic (p. 4, ¶0019).

Accordingly, Collas *et al.* teach the claimed invention.

Claims 24, 25 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Vanderzwalmen *et al.* (**Hum. Reprod.**, 7(4): 537-544 (1992)).

The claims are directed to animals produced by methods of nuclear transfer, and specifically humans. The claims are product by process claims. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). Further, see MPEP §2113, "Even though product-by process

claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." Thus, art that teaches a human anticipate these claims.

Vanderzwalmen *et al.* teach women undergoing IVF treatment and men donating semen for this treatment. See page 538, IVF Procedures. Thus, because the claims read on humans, Vanderzwalmen anticipate the claimed invention.

Claims 24-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Thomson (**U.S. Pat. No. 5,843,780,** issued December 18, 1996, Reference A1 on Applicants' IDS, filed 9/2/04).

The claims are directed to animals produced by methods of nuclear transfer, and specifically non-human primates. The claims are product-by-process claims (see above). Thus, art that teaches non-human primates anticipates these claims.

Thomson teaches the isolation of rhesus embryos from a rhesus monkey (see col. 13, lines 60-65). Thus, because Thomson teach a rhesus monkey, they anticipate the claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Thursday from 7:00 to 5:00 (Eastern Standard Time). Should the Examiner be unavailable, inquiries should be directed to Ram Shukla, SPE of Art Unit 1632, at (571) 272-0735. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the Official Fax at (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

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